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SPECIAL ARTICLE

Mesothelioma Trends in the United States: An Update Based on Surveillance, Epidemiology, and End Results Program Data for 1973 through 2003

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Using 1973–2000 mesothelioma incidence data released by the Surveillance, Epidemiology, and End Results Program in April 2003, the authors estimated the parameters of a birth-cohort and age model to determine whether previously reported patterns of mesothelioma in the United States have changed. Compared with analyses based on data through 1992, a slower decline was found in male cases immediately after a peak in 2000–2004, but no other notable changes in the time pattern were detected. Analysis confirmed that the annual number of male mesothelioma cases, which increased steeply from the 1970s through the mid-1990s, has leveled off in terms of both the age-adjusted rate and the absolute numbers of cases. After a peak of approximately 2,000 cases, a return to background levels is expected by 2055. The total projected number of male mesothelioma cases in 2003–2054 is approximately 71,000. The maximum lifetime risk for males, which occurs for the 1925–1929 birth cohort, is 1.8×10^{-3}. The age-adjusted rate for females is constant, as are the female lifetime mesothelioma risk across birth cohorts (3.6×10^{-4}) and the annual risk (3.9×10^{-6}). The time pattern of cases for females supports the existence of a threshold exposure for mesothelioma and a quantifiable background rate.

asbestos; incidence; mesothelioma

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.

Mesothelioma incidence often is interpreted as an indicator of exposure to asbestos. Projections of the number of mesothelioma cases over time may be used to evaluate various asbestos health management interventions including exposure limits and products bans. Mesothelioma projections also provide a foundation for estimating the number of potential lawsuits from persons claiming occupational exposure to asbestos or exposure resulting from use of previously manufactured asbestos-containing products. Noting recent publications discussing mesothelioma incidence in North America and that projected numbers of future mesothelioma cases in the Netherlands, Sweden, and the United Kingdom have been adjusted based on new data (1–4), we analyzed current Surveillance, Epidemiology, and End Results (SEER) Program data (5) to update mesothelioma trends in the United States.

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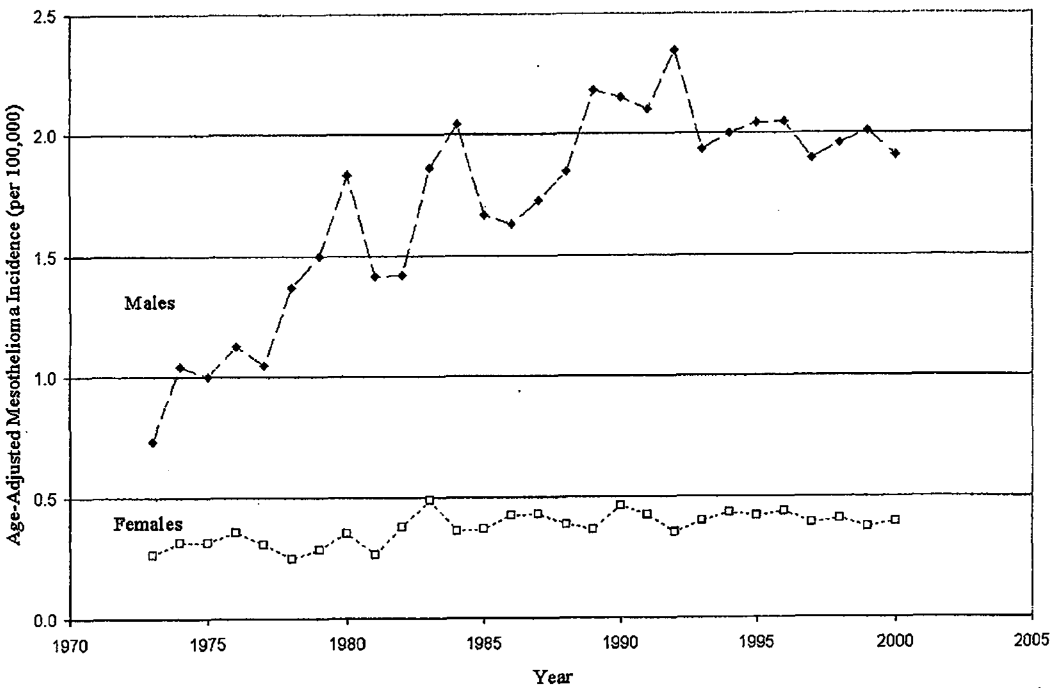

FIGURE 1. Age-adjusted incidence rates of mesothelioma (pleural + peritoneal) in the United States based on Surveillance, Epidemiology, and End Results Program data released in April 2003.

MATERIALS AND METHODS

We applied maximum likelihood estimation (6) to SEER data (5) to estimate the parameters of a birth-cohort and age model (7). The SEER database contains information on cancer incidence in the United States by year of diagnosis and age from nine cancer registries for 1973 through 1991 and 11 registries for 1992 through 2000. The SEER registries represent 14 percent of the US population, are similar to the United States regarding measures of poverty and education, and tend to be more urban than the general US population (8–10). For males and females, we extracted counts of mesothelioma cases and corresponding population counts for each year and each 5-year age interval from 0–4 through 85 years or older. These data were realigned into 5-year birth-cohort categories (1885–1889 through 1970–1974).

Incidence estimates calculated from the model were combined with mortality rates for all causes in a survival analysis to calculate, for each birth cohort, the probability of mesothelioma occurring in each 5-year age interval, conditioned on cancer-free survival to that age interval (11). These probabilities were used to calculate the lifetime risk of mesothelioma for each birth cohort.

For all-cause mortality, we created a table of cohort mortality rates by 5-year age interval for each birth cohort. The cohort mortality rates were developed from two sources: 1) cross-sectional mortality rates for 5-year age intervals from the SEER system, years 1969–2000 (12); and 2) cross-sectional mortality rates by 10-year age intervals for individual years 1900 through 1968 (13). We factored the 10-year age intervals into two 5-year intervals and then realigned the results to form a table of cohort mortality rates for birth cohorts 1900–1904 through 1995–1999.

To project the annual number of future mesothelioma cases, we required natality data (14), mesothelioma probabilities for each age interval, and all-cause mortality rates for future birth cohorts. The number of births for all future birth cohorts was set equal to the number of births reported for the most recent birth cohort, 1995–1999.

Future birth-cohort mesothelioma probabilities for females, starting with the 1965–1969 cohort, were set to the average of past probabilities for females, which have been relatively constant since the 1900–1904 birth cohort. Mesothelioma probabilities for males have been declining toward those for females. Therefore, probabilities for males in future birth cohorts starting with 1965–1969 were set equal to the averages for females, which we interpreted as background rates for mesothelioma. All-cause mortality rates for the year 2000 were used for all future birth cohorts.

RESULTS

Trend in age-adjusted rates

The age-adjusted incidence (figure 1) indicates a consistently higher rate for males versus females across all years,

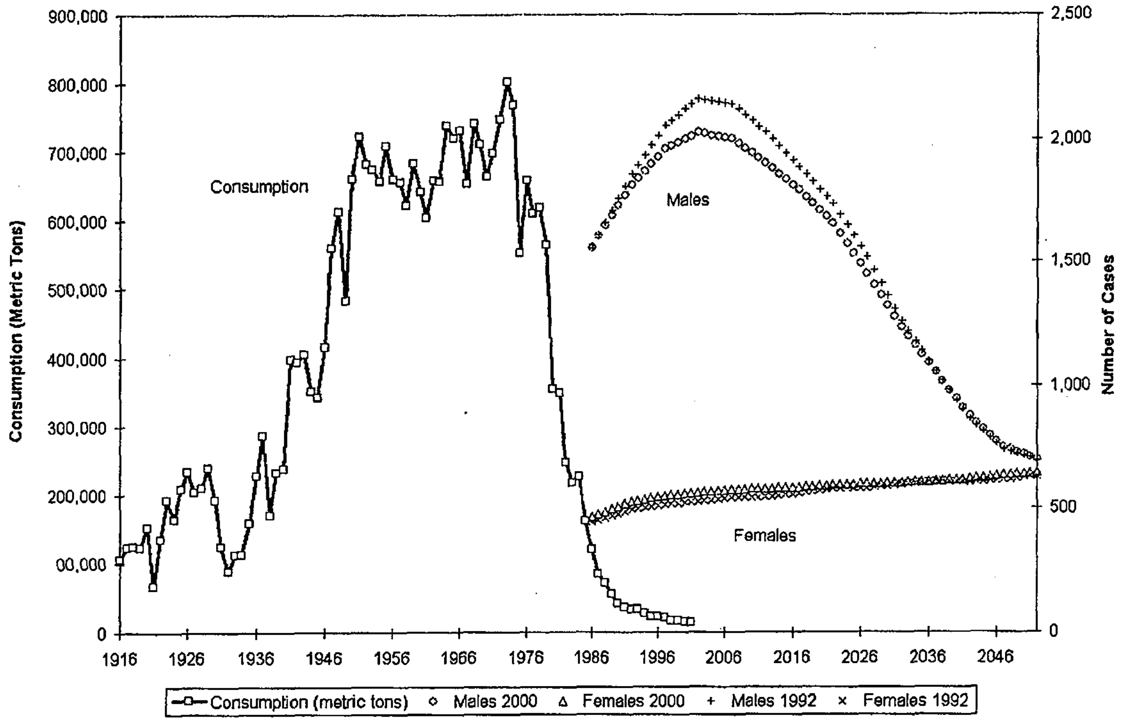

FIGURE 2. Asbestos use (consumption) in the United States and projected numbers of male and female mesothelioma cases based on a birth-cohort and age model estimated from Surveillance, Epidemiology, and End Results (SEER) Program data for two periods, 1973–1992 and 1973–2000.

an increasing trend over the years for males, and a virtually constant rate for females. Accounting for a latency period of 20–40 years for mesothelioma, the increased incidence for males reflects the increased use of asbestos (15) in the United States (figure 2) and the high levels of occupational exposure prior to the late 1960s, when formal workplace exposure limits were established. The age-adjusted rate for males was flat from 1990 through 2000. Projections of future male mesothelioma cases, discussed later, indicate that the number of male cases per year has peaked and is declining.

Comparison of trends: data for 1973–1992 versus 1973–2000

A direct comparison of mesothelioma trends based on current data with trends published by Price (7) would not be meaningful because the SEER data have changed since 1992. Two registries were added starting with 1992 data, and mesothelioma counts for the years 1973 through 1991 have been corrected. Therefore, our modeling is based on the current SEER database, first using cases diagnosed from 1973 through 1992 and then using all cases, 1973 through 2000.

Model fits

For each data set (males, females; two time intervals), the predicted values tracked the observed values reasonably well, although there were a few data points with large deviances. The 1973–1992 data sets had 80 data points; the 1973–2000 data sets had 101 data points. When the large deviances were excluded, the statistical fits were acceptable ($p > 0.05$ based on total deviance) for each model. The numbers of data points remaining were, for 1973–1992, 79 for males and 80 for females and, for 1973–2000, 92 for males and 99 for females.

Lifetime risk of mesothelioma

For females, the lifetime risk of mesothelioma is approximately constant at 3.6×10^{-4} (figure 3). The lifetime risk for males (1973–1992 data, not shown) is a maximum of 2.1×10^{-3} for the 1925–1929 birth cohort and then declines sharply for subsequent cohorts, except for an isolated increase for the 1940–1944 cohort. Regarding the 1973–2000 data, the maximum risk is 1.8×10^{-3} (figure 3). The trend is relatively flat before starting downward after the 1940–1944 cohort.

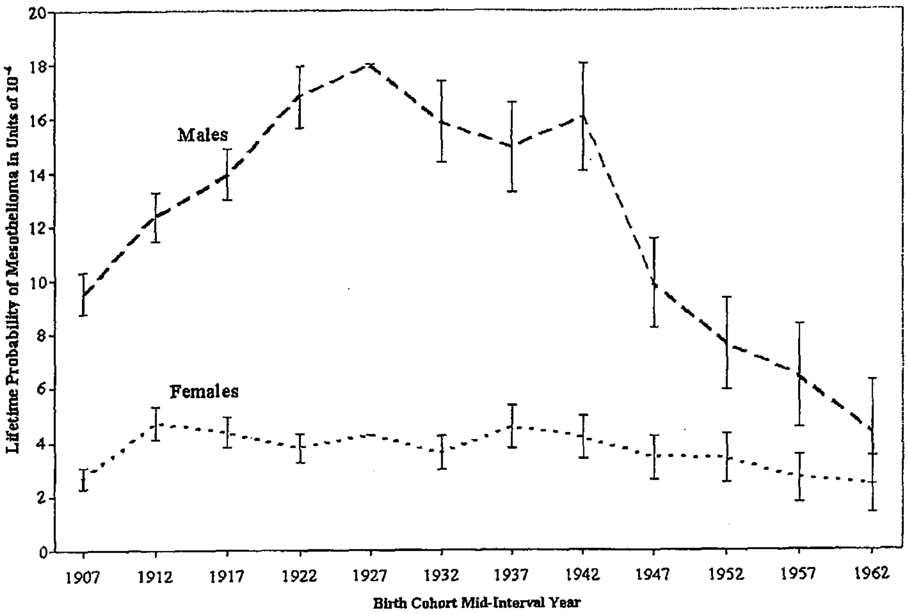

FIGURE 3. Lifetime probability (risk) of mesothelioma (pleural + peritoneal) and 95% confidence intervals (vertical bars) based on a birth-cohort and age model estimated from 2003 Surveillance, Epidemiology, and End Results Program data covering 1973–2000.

Projected number of mesothelioma cases

For the two data sets, mesothelioma projections for females (figure 2) are virtually identical. Although the age-adjusted rate for females is constant, the number of mesothelioma cases increases slightly over time as a function of population size and shifting age distribution. Currently (2003), the annual estimate of female mesothelioma cases is approximately 560.

The trend for males in both data sets peaks in the 2000–2004 time frame at slightly more than 2,000 mesothelioma cases (figure 2). The 1973–2000 model shows fewer mesothelioma cases than the 1973–1992 model during the peak years, but not overall. The total numbers of male mesothelioma cases projected for 2003 through 2054 are 70,990 for the 1973–2000 data and 73,892 for the 1973–1992 data.

DISCUSSION

Overall, there have been no substantive changes in the time pattern of mesothelioma incidence in the United States since 1992. This conclusion would not be apparent if the current results using SEER data for 1973–2000 were compared with the results published by Price (7) that were based on SEER data for 1973 through 1992. That estimated model (7) showed a sharper decline in the number of annual male mesothelioma cases, projecting approximately 7,000 fewer cases between 2003 and 2054, than the model based on the most current data. However, a comparison to the Price results (7) would not be meaningful because of changes in SEER data and application of the cohort mortality rates used here. Therefore, it was necessary to reestimate the model using revised data through 1992 for comparison to the model based on current data through 2000. This comparison indicated no substantive change in the time pattern or number of future cases.

In addition to describing the time pattern of mesothelioma incidence, our results contain information about the potential effects of environmental exposures to asbestos and two related issues: 1) the existence of an exposure threshold and 2) the existence and magnitude of a background rate (i.e., mesotheliomas not associated with asbestos exposure). (In this discussion, threshold does not mean an exposure below which the risk of mesothelioma is zero; the threshold is an asbestos exposure level associated with a negligible incremental risk of mesothelioma.)

The constancy alone of the mesothelioma risk for females over time supports the existence of a threshold exposure. The effects, if any, of environmental exposures for the US population as a whole cannot be observed for males; as a group, males experienced high occupational exposures that masked low-exposure effects. In contrast, female exposures to asbestos have been primarily environmental. In the 1930s through the 1960s, women generally did not work in industries in which men experienced high levels of exposure to asbestos. For some women, exposures have been domestic (i.e., they live in households with men who were exposed

occupationally), but the number of women with high levels of domestic exposure, although not zero, would have been relatively small. However, all women were exposed to asbestos in the environment, an exposure that would have increased since the 1930s, especially the dramatic increase during the 40-year period from 1930 to 1970 in the amount of asbestos used in US products (figure 2). As use increased, higher environmental exposures would have resulted from asbestos mining, manufacturing, and product use (e.g., vehicle brake systems, construction materials, and other asbestos-containing products) during this period and beyond for as long as the asbestos-containing products were in use.

Nevertheless, the mesothelioma risk for women has not increased. The age-adjusted mesothelioma rate for females was constant at an average of approximately 0.30 per 100,000 between 1973 and 1982, when it showed a one-time increase to 0.40 per 100,000 (figure 1). One might be tempted to interpret this change as a response to increasing environmental exposure. However, the female rate, which should have continued to increase after 1982 if the environmental exposure explanation is correct, remained constant after 1982. Therefore, the one-time mesothelioma increase for females does not indicate increasing exposure to asbestos in the environment but more likely a diagnostic effect. Environmental exposure levels, although increasing, have not triggered a risk response in women. Therefore, those exposure levels must have been below a threshold for mesothelioma.

A threshold higher than typical environmental asbestos exposures, as argued above, implies the existence of background mesotheliomas caused by agents other than asbestos that could account for most, if not all, female cases of mesothelioma. A number of studies provide evidence of background mesotheliomas (16–28). Simian virus 40 (SV40) is one of the nonasbestos agents that has been identified as a possible cause of mesothelioma (29, 30). Simian virus 40 was a contaminant in polio vaccines administered to 10–30 million people in the United States, mostly children, between 1955 and 1963 (30). It has not been determined whether simian virus 40 acting alone can cause mesothelioma (30). Our analysis does not indicate an increased risk in the 1955–1959 or 1960–1964 birth cohorts, those most likely to have received the contaminated vaccine (refer also to Strickler et al. (31)).

If all female cases of mesothelioma were unrelated to asbestos exposure, our analysis indicates that the lifetime background risk would be 3.6×10^{-4} (figure 3) and the current annual risk would be approximately 4 per million (over 5 per million if the population at risk is aged ≥20 years). These background risk levels would be upper bounds if a portion of female cases of mesothelioma were due to occupational, domestic, or unique high environmental exposures.

The background rates for females may not apply directly to males because the percentages of pleural and peritoneal mesotheliomas are different for men and women. In the SEER database, peritoneal mesotheliomas account for 7 percent of all mesotheliomas in males but 17 percent of all mesotheliomas in females. It is possible that peritoneal mesotheliomas in women are of two types but cannot be distinguished histologically: 1) those that are similar to mesotheliomas in males and 2) those that are unique, as evidenced in part by longer survival times of the cases (32; Andrew Churg, University of British Columbia, personal communication, 2002). On the basis of the differences between cases of mesothelioma in males and females, an adjustment to the background rates suggested above for females would be required if they were to be applied for males. For example, if all peritoneal mesotheliomas in females were excluded, the annual background rate for males would be 83 percent of the background rate for females.

The mesothelioma epidemic in the United States, which is beginning to recede, has been a consequence of ongoing high-level occupational exposure to asbestos from the 1930s through the 1960s in workplaces populated almost exclusively by males. Asbestos regulations promulgated by the US Occupational Safety and Health Administration (OSHA) in the early 1970s have led to dramatic reductions in exposure. These reductions are reflected in the pattern of mesothelioma incidence in the SEER data and were magnified through our modeling and analysis. It is unlikely that low environmental exposure to asbestos, or any other type of low-level asbestos exposure, is associated with more than a negligible risk of mesothelioma.

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